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MATHEMATICAL MODELING OF THE RESPIRATORY PROCESS AND TRANSPORT OF OXYGENATED BLOOD TO THE CELLS OF THE HUMAN ORGANISM

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ABSTRACT

In this article, a study is made of the main characteristics and functions of the cardiovascular system and the lungs, indicating how they unite to be able to bring oxygenated blood to the different cells of the human organism, as well as other essential nutrients for the harmonious functioning of our body; In addition, the main diseases that can affect these organs and the causes that could cause them are indicated. A model is made by means of differential equations of the blood oxygenation process and by means of a qualitative study conclusion are given, predicting the future behavior of the process.

KEYWORDS: Mathematical modeling. the lungs, cardiovascular system.

1. INTRODUCTION

Breathing is a basic and automatic mechanism of the human body, with several functions. In addition to allowing gas exchange between the body and the environment, it helps to strengthen muscles and keep the brain healthy. The human body performs two types of breathing, cellular and pulmonary. The first is a process that takes place inside the cells and is responsible for obtaining energy. The second, in turn, is responsible for providing oxygen for the cells to carry out cellular respiration and remove the carbon dioxide resulting from this process from our body; here are involved the cardiovascular system and the lungs, each one with its functions in this process [15].

The cardiovascular system is the system responsible for ensuring the transport of blood throughout the body, thus allowing our cells to receive, for example, nutrients and oxygen. This system is formed by the heart and blood vessels; the human heart, like that of other mammals, is a muscular organ made up of four

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chambers: two atria and two ventricles. The atria are the chambers responsible for ensuring the reception of blood in the heart, while the ventricles are the chambers responsible for ensuring the pumping of blood out of the heart. On the left side of the heart, only oxygen-rich blood is present, while on the right side, only blood rich in carbon dioxide is observed. In the heart, there is also the presence of four valves that prevent the backflow of blood, thus allowing a continuous flow [11].

The heart is able to contract and also to relax, the contraction being called systole and relaxation of diastole. When it contracts, it pumps blood and when it relaxes, it fills with blood. In humans, heartbeats originate in the heart itself. The region that originates the heartbeat is called the sinoatrial node and it is characterized by being a cluster of cells that produce electrical impulses.

A heart murmur is a noise caused by the turbulent flow of blood, which is usually heard during a routine examination through a stethoscope. In general, we can classify heart murmurs as innocent or pathological. Innocent heart murmurs, also called functional murmurs, are those that are not related to pathologies and also do not require any type of treatment. They occur due to a turbulent flow of blood which, in this case, does not present physical changes in the heart. This type of murmur can be the result of some disease that is not related to heart problems, such as fevers and anemia, or it can also arise after physical exercises. Pathological murmurs, unlike innocent murmurs, are the result of heart problems, such as changes in heart valves. They can be congenital or acquired and are usually accompanied by tiredness and chest pain. These murmurs can be the result, for example, of an arctic stenosis or valvular insufficiency [12].

Arteries are blood vessels that transport blood from the heart to the tissues. In arteries, the blood is under high pressure and, for this reason, these blood vessels have very resistant walls. Contrary to what many people think, arteries do not transport only oxygen-rich blood (arterial blood), being observed the transport of oxygen-poor blood (venous blood) in the pulmonary artery. Arteries are blood vessels that have thick and resistant walls to support the high-pressure blood that flows through them. The function of these vessels is to allow the blood that leaves the heart to be carried to the different tissues of the body [11], [14].

Atherosclerosis is a disease that affects the arteries of the body and is characterized by the deposit of fat, calcium and other elements in the walls of these blood vessels, forming plaques called atheromas. This deposition occurs slowly and initially causes no symptoms. As the disease progresses, however, the caliber of the arteries becomes reduced, which prevents blood supply to the part of the body that is supplied by that artery. The symptoms of atherosclerosis depend on the artery being affected. When it compromises the arteries of the heart, for example, it can cause angina (chest pain). There are several risk factors for

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the development of atherosclerosis, some of which are high levels of lipids in the blood (dyslipidemia) and hypertension.

A cerebrovascular accident (CVA) occurs when an area of the brain does not receive blood properly. This problem can occur as a result of the rupture of an artery or even its obstruction. When an artery in the brain region is blocked, preventing blood flow, we have a so-called ischemic stroke. When the artery ruptures, we have a so-called hemorrhagic stroke. Tingling in the face, changes in speech and vision, change in balance, dizziness, weakness and sudden headache are symptoms that can arise in cases of stroke. Hypertension, high cholesterol, smoking and advanced age are risk factors for the development of the problem [11], [14].

Veins result from the convergence of capillaries and become larger as they get closer to the heart. Unlike arteries, the tunica media of veins has fewer muscles and elastic fibers, and blood pressure in these vessels is low. The main task of the veins is to carry blood from the body to the heart so that it can be pumped back into the body. As some veins carry blood against gravity and blood pressure is low, these structures have some valves. These valves, formed by folds of the tunica intima, ensure the correct flow of blood towards the heart. Capillaries are very thin blood vessels, lacking the tunica media and adventitia, which form a complex network of vessels. Because they have a thin wall, with only a few layers of cells, they become an ideal place for gas exchange to occur [14].

Blood capillaries are extremely important vessels for the functioning of our body, as they allow the exchange of substances between the blood and adjacent tissues. It is through the capillaries, therefore, that the cells are able to receive oxygen and the nutrients necessary for their functioning. The exchange of substances through these blood vessels can occur between and across cells. In capillaries that have pores, the transfer of substances can also occur through them [14].

Red blood cells, also called erythrocytes and red blood cells, are circular cells responsible for transporting oxygen throughout our body. These cells have the characteristic of being anucleated when mature. After losing their core, they acquire a biconcave shape. Hemoglobin, the protein that gives blood its color and acts to transport oxygen, is found inside red blood cells; when there is a decrease in the synthesis of red blood cells, an increase in their rate of destruction, production of deficient red blood cells, blood loss or even a reduction in the production of hemoglobin, we have anemias. Hemoglobin has a higher affinity for carbon monoxide than for oxygen, when this combination occurs, oxygen cannot be transported by hemoglobin, thus causing a deficiency in oxygenation of body tissues. This problem is serious and can cause respiratory distress, headache, visual changes, tachycardia, syncope and even death.

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The process of red blood cell production, called erythropoiesis, occurs in the red bone marrow and is regulated by erythropoietin, a hormone produced in the kidneys in adults [10]. Hypoxia (low oxygen concentration) is a great stimulator of the production of this hormone. At high altitudes, for example, erythropoietin is produced in large amounts, thus initiating an increase in red blood cell production. It is common for athletes to train in high-altitude places so that there is a greater production of erythropoietin, so the production of red blood cells increases and, consequently, their ability to transport oxygen to the tissues also increases. This is known as altitude training, which makes these athletes perform better in competitions such as running and cycling [13].

Anemia is defined by the World Health Organization (WHO) as a condition in which the hemoglobin content of the blood is below normal as a result of a lack of one or more essential nutrients. Anemias can be caused by a deficiency of several nutrients such as iron, zinc, vitamin B12 and proteins [17].

The lungs are attached to the pericardium through pulmonary ligaments and to the trachea and heart by structures called the hilum, comprising pulmonary vessels, lymphatic vessels, bronchial vessels, main bronchi and nerves that enter and leave the lungs. The lungs are covered by a thin layer, the pleura, which consists of a thin, transparent membrane. The inner pleura is attached to the lung surface, and the outer pleura is attached to the chest wall. In the intermediate space of the pleura there is a reduced space, occupied by a lubricating liquid secreted by the pleura, this liquid is what keeps the two pleurae together, due to surface tension, causing them to slide during respiratory movements [4], [5].

The base of each lung rests on the diaphragm, the organ that separates the thorax from the abdomen, present only in mammals; promoting, together with the intercostal muscles, respiratory movements. In the lungs, the bronchi branch intensely, giving rise to increasingly thin tubes, the bronchioles. The highly branched set of bronchioles is the bronchial tree or respiratory tree.

In pulmonary respiration, air enters and leaves the lungs due to the contraction and relaxation of the diaphragm. When the diaphragm contracts, it decreases the pressure in the lungs and the air that is outside the body enters rich in oxygen; process called inspiration. When the diaphragm relaxes, the pressure inside the lungs increases and the air that was inside now leaves with carbon dioxide; process called expiration. People can stop breathing, but no one can go without breathing for more than a few minutes, because the concentration of carbon dioxide in the blood gets so high that the body can no longer supply energy to the cells and the medulla, part of the nervous system that forms the brain [15].

The person may suffer from different lung diseases such as bronchitis, tuberculosis, pulmonary emphysema, pneumonia, asthma, lung cancer, etc. When inflammation of an individual's lungs, more specifically the alveoli, occurs, we call it pneumonia, due to infection caused by bacteria, viruses, fungi and other infectious agents. Pneumonia can cause death if left untreated; these diseases can damage the pulmonary alveoli, decreasing the lung's ability to perform its function [1], [6], [8], [9].

The main purpose of the lungs is to supply our blood with oxygen, which is transported to the cells of the body. Respiratory movement is controlled by a nerve center located in the spinal cord; under normal conditions, this center produces an impulse every five seconds, stimulating contraction of the thoracic muscles and diaphragm, where we inhale. However, when the blood becomes more acidic due to the increase in carbon dioxide, the medullary respiratory center induces the acceleration of respiratory movements.

In case of a decrease in the concentration of oxygen gas in the blood, the respiratory rate is also increased; this reduction is detected by chemical receptors located on the walls of the aorta and carotid artery; when the air enters or leaves the body through the mouth, however, the humidification and heating of the air are incomplete, with no filtration of dust particles, smoke, and even microscopic living beings, such as viruses and bacteria, capable of causing damage to our health. Some impurities are "filtered" in various organs of the respiratory system, but others manage to pass to the lungs, causing diseases.

Humans have neurons in the medulla region that ensure the regulation of breathing. The medulla then senses these changes, and signals are sent to the intercostal muscles and diaphragm to increase the intensity and rate of respiration. When the pH returns to normal, there is a reduction in respiratory rate and intensity. It is worth noting that changes in the level of oxygen in the blood trigger few effects in the bulb. However, when levels are too low, the respiration rate increases. [7].

Several works, books and articles referring to processes in human life are known; Among these books dedicated to mathematical modeling, the following [2] and [3] are indicated in which real problems are simulated using differential equations and systems of equations, where in addition a certain treatment is carried out to reach conclusions of the processes, in particular the blood oxygenation problem. In [3] different real-life problems are treated by means of equations and systems of differential equations, all of them only in the autonomous case; where, in addition, examples are developed, and problems and exercises are placed so that they can be developed by the reader. The authors of [2] indicate a set of articles forming a collection of several problems that are modeled in different ways, but in general the qualitative and analytical theory of differential equations are used both in the autonomous and non-autonomous cases.

Systemic circulation or large circulation is the circuit that blood makes from the heart towards the various tissues of the body and then returning to that organ. Upon reaching the lung, the blood is propelled to the body. In the capillaries, gas exchange takes place, and the blood, now rich in carbon dioxide and poor in oxygen, returns to the heart. Pulmonary circulation or small circulation is the circuit carried out by blood from the heart to the lungs and its return to the heart. In this circuit, the oxygen-poor blood leaves the heart, travels to the lung, where it is oxygenated, and returns to the heart [17].

MODEL FORMULATION

In order to simulate the process of oxygenation of blood through the lungs and its transport to the cells via the cardiovascular system, it is necessary to consider some basic principles; first, that the lung does not receive more oxygen than our body needs, therefore, its variation will increase proportionally to its concentration up to certain limits; decreases proportionally to the concentration of carbon dioxide and decreases proportionally to the square of its own concentration, because in this way it will grow to an ideal value and will not be added from there, here it influences that hemoglobin has a greater affinity for carbon monoxide than for oxygen, causing deficiency in the distribution of oxygen, among other facts. But in the variation of carbon dioxide, it is necessary that it is added proportionally to the concentration of oxygen and decreases proportionally to its concentration, because our organism does not accept high concentrations of carbon dioxide.

To formulate the model, a system of differentiable equations will be used, for which the following unknown functions will be introduced:

$\varkappa_1$ é a concentração total de oxigênio no sangue no momento t.

$\varkappa_2$ is the total concentration of carbon dioxide in the blood at the time t.

Furthermore, $\overline{x}_1$ and $\overline{x}_2$ are the ideal values of oxygen and carbon dioxide in the human body, respectively.

To write the system, the variables are defined x_1 and x_2 as follows: $x_1 = \varkappa_1 - \overline{x}_1$ and $x_2 = \varkappa_2 - \overline{x}_2$ so if $x_1 \to 0$ and $x_2 \to 0$ if you would have to, $\varkappa_1 \to \overline{x}_1$ and $\varkappa_2 \to \overline{x}_2$, which would constitute the main objective of this work. Therefore, the model will be given by the following system of equations,

$$\begin{cases} x_1' = a_1 x_1 - a_2 x_2 - a_3 x_1^2 + X_1(x_1, x_2) \\ x_2' = a_4 x_1 - a_5 x_2 + X_2(x_1, x_2) \end{cases} \qquad (1)$$

The functions $X_i, (i = 1{,}2)$ are power series converging in a neighborhood of the origin of coordinates, which represent external perturbations or the process itself, which at a given moment could change the behavior, these functions have the form,

$$X_i(x_1, x_2) = \sum_{|p| \geq 2} X_i^{(p)} x_1^{p_1} x_2^{p_2} \ (i = 1{,}2), |p| = p_1 + p_2$$

The coefficients (a_i) $(i = 1{,}2{,}3{,}4{,}5)$ have the following meaning in the system (1):

a_1 represents the coefficient of the increase of oxygen with respect to its own concentration.

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a_2 represents the coefficient of the decrease of oxygen in relation to the concentration of carbon dioxide.
a_3 represents the coefficient of the decrease of oxygen with respect to the square of its own concentration.
a_4 represents the coefficient of increase of carbon dioxide in relation to the concentration of oxygen.
a_5 represents the coefficient of decrease of carbon dioxide with respect to its own concentration.

The characteristic equation of the matrix of the linear part of the system (1) has the following form,

$$\lambda^2 + (a_5 - a_1)\lambda + (a_2 a_4 - a_1 a_5) = 0 \quad (2)$$

Theorem1: The conditions $a_5 > a_1$ and $a_2 a_4 > a_1 a_5$ are necessary and sufficient for the asymptotic stability of the null solution of system (1).

The demonstration of this result is a direct consequence of the Hurwitz conditions and stability by the first approximation.

Note1: If the conditions are met $a_5 > a_1$ and $a_2 a_4 > a_1 a_5$ the total concentrations of carbon dioxide and oxygen converge to the ideal values for the proper functioning of the human body.

Suppose that $a_5 = a_1$ and $a_2 a_4 > a_1 a_5$, if you have a pair of pure imaginary eigenvalues σi and $-\sigma i$, this makes it impossible to act as before; by means of a non-degenerate linear transformation $X = SY$, the system (2) can be transformed into the system,

$$\begin{cases} y_1' = \sigma i\, y_1 + Y_1(y_1, y_2) \\ y_2' = -\sigma i y_2 + Y_2(y_1, y_2) \end{cases} \quad (3)$$

Here, the Analytical Theory of Differential Equations will be used to reduce the system (3) to a simpler force that allows the study of its trajectories. Where $y_2 = \bar{y}_1$ how it is $Y_i, (i = 1,2)$ they are power series; system (3) is a critical case, for which the first approximation method cannot be applied, in which case the second Liapunov method will be applied once this system is reduced to normal form.

Theorem 2: The change of variables,

$$\begin{cases} y_1 = z_1 + h_1(z_1, z_2) \\ y_2 = z_2 + h_2(z_1, z_2) \end{cases} \quad (4)$$

transform system (3) into normal form,

$$\begin{cases} z_1' = \sigma i z_1 + z_1 P(z_1 z_2) \\ z_2' = -\sigma i z_2 + z_2 \overline{P}_2(z_1 z_2) \end{cases} \quad (5)$$

Where $h_i, i = 1,2$ P and $\bar{P}$ are power series.

Proof: Deriving the transformation (4) along the trajectories of systems (3) and (5) we obtain the system of equations,

$$\begin{cases}(p_1-p_2-1)\sigma i h_1+z_1P=Y_1-\frac{\partial h_1}{\partial z_1}z_1P-\frac{\partial h_1}{\partial z_2}z_2\overline{P}\\(p_1-p_2+1)i\sigma h_2+z_2\overline{P}=Y_2-\frac{\partial h_2}{\partial z_1}z_1P-\frac{\partial h_2}{\partial z_2}z_2\overline{P}\end{cases} \quad (6)$$

The system (6) allows determining the coefficients of the series, h_1, h_2, P and $\overline{P}$; the resonance equations are of the system are, $p_1-p_2-1=0$ and $p_1-p_2+1=0$; with what P and $\overline{P}$ are different from zero in the resonant case, with h_1 and h_2 are arbitrary, but by the uniqueness of the solutions they are taken equal to zero in this case, and by the resonance equations the forms of the powers of P and $\overline{P}$. In the non-resonant case, the series are taken P and $\overline{P}$ are considered equal to zero and in this case h_1 and h_2 are uniquely determined.

The series P and $\overline{P}$ admit the following development in power series,

$$P(z_1z_2)=\sum_{n=k}^{\infty}a_n(z_1z_2)^n+\sum_{n=l}^{\infty}b_n(z_1z_2)^n$$

Theorem 3: If $a_k<0$, then the trajectories of system (5) are asymptotically stable, otherwise they are unstable.

Proof: Consider the positive definite Lyapunov function,

$V(z_1,z_2)=z_1z_2$

The function V is such that its derivative along the paths of system (5) has the following expression,

$V'(z_1,z_2)=a_k(z_1z_2)^{k+1}+R(z_1,z_2)$

It can be seen that the derivative $V'(z_1,z_2)$ is negative definite, because in the function $R(z_1,z_2)$ only have terms with a degree higher than $2(k+1)$, so it will represent an infinitesimal of higher order and the sign of V' is determined by the sign of a_k. That together with what $V(z_1,z_2)$ is positive definite guarantees the asymptotic stability of the null solution of system (5).

Note 2: If $a_k<0$, so, still being a critical case, the concentrations of oxygen and carbon dioxide in the blood converge to the optimal values, constituting in this case a person in a healthy state that has no affectations in the respiratory process.

Example: Let the following system of equations, which models blood oxygenation,

$$\begin{cases}x_1'=x_1-2x_2-10^{-2}x_1^2-10^{-3}x_1x_2^2\\x_2'=x_1-x_2-10^{-3}x_1^2x_2\end{cases}$$

as can be seen, meet the conditions to constitute a critical case, since its eigenvalues are $\lambda_1=i$ and $\lambda_2=-i$.

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The graphs of their trajectories are presented below.

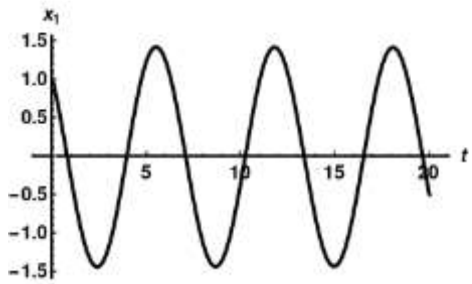

Fig.1: Graph of x_1 with respect to time.

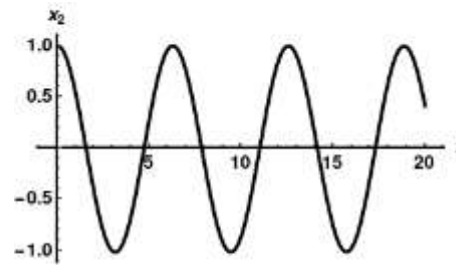

Fig.2: Graph of x_2 with respect to time.

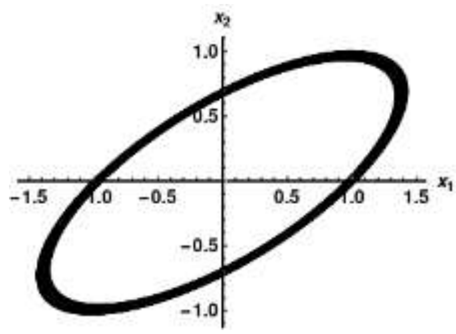

Fig.1: Graph of $x_2$with relation x_1.

Observation3: It can be seen that the trajectories have a periodic behavior, this corresponds to the cyclic process that characterizes the problem of blood oxygenation through the lungs.

III. CONCLUSIONS

1. The problem of studying the respiratory process is increasingly a problem of current and transcendental importance because there are many people in the world with affectations in this sense.
2. Environmental problems make it increasingly important to reach conclusions with some information from a patient, who would be in charge of mathematical modeling.
3. Theorem 1 gives necessary and sufficient conditions for the total concentrations of oxygen and carbon dioxide to converge to the optimal values, making the person comfortable.

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4. The critical case of a pair of pure imaginary eigenvalues, considered in this work, is absolutely possible and therefore its study is important not only from a theoretical point of view.
5. Theorem 2 allows to transform the system (3) in the normal form, which facilitates the qualitative study to reach conclusions regarding the future situation of our planet.
6. In theorem three, conditions are reached that allow us to guarantee that even in the critical case it can be concluded that the values of the concentrations of oxygen and carbon dioxide will converge to the ideal values in our organism.
7. The example developed, which of course refers to a healthy patient modeled by a system that represents a critical case, represents another form of diagnosis based on the rhythmic characteristics of the problem studied, as the arrhythmia would indicate changes in the process and therefore the call for attention as the patient's health.

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